Hospital Library

VOLUME LXXV NUMBER 3

BULLETIN of the JOHNS HOPKINS HOSPITAL

THE PUBLICATION OF THE MEDICAL SCHOOL AND HOSPITAL
SUPPORTED BY THE DE LAMAR FUND OF THE JOHNS HOPKINS UNIVERSITY

September, 1944

"Rights, Honors and Privileges thereto Appertaining." ALAN M. CHESNEY 149

Studies on Fracture Convalescence. I. Nitrogen Metabolism after Fracture and Skeletal Operations in Healthy Males. JOHN EAGER HOWARD, M.D., WILLIAM PARSON, M.D., KAY EISENBERG STEIN, HARRY EISENBERG AND VIRGINIA REIDT 156

Infestation of the Genito-Urinary Tract by Strongyloides Stercoralis: A Case Report. RICHARD WHITEHILL, MAJOR, M.C., AUS AND MITCHELL H. MILLER, CAPT., M.C., AUS 169

The Utilization of *d*-Amino Acids by Man. I. Tryptophane, Methionine and Phenylalanine. ANTHONY A. ALBANESE. With the technical assistance of JANE E. FRANKSTON, VIRGINIA IRBY AND DOROTHY L. WAGNER 175

Nephrectomy for Hypertension in a 2½ Year Old Child with Apparent Cure for 3 years. JAMES H. SEMANS, 1ST LT., M.C., A.U.S. 184

Book Reviews 193

PUBLISHED MONTHLY

THE JOHNS HOPKINS PRESS, Baltimore-18, Maryland

Made in United States of America

COPYRIGHT, 1944, BY THE JOHNS HOPKINS PRESS

THIS JOURNAL IS
MANUFACTURED UNDER WARTIME CONDITIONS
IN CONFORMITY WITH ALL GOVERNMENT
REGULATIONS CONTROLLING THE USE OF
PAPER AND OTHER MATERIALS

BULLETIN
OF
THE JOHNS HOPKINS HOSPITAL

MANAGING EDITOR, L. EMMETT HOLT, JR.

ASSOCIATE MANAGING EDITOR, JOHN A. LUETSCHER, JR.

EDITORIAL BOARD

E. Cowles Andrus
Charles R. Austrian
W. Halsey Barker
James Bordley, III
Chalmers L. Gemmill
Arnold R. Rich

All correspondence relating to the publication of papers should be addressed to The Editor, Bulletin of The Johns Hopkins Hospital, Baltimore-5, Md.

Books for review should be sent to The Editor at the above address.

Twenty-five reprints, without covers, of articles will be furnished to contributors free of cost. An order slip for additional reprints, with a table showing cost, is sent with proof.

Correspondence concerning business matters should be sent to The Johns Hopkins Press, Baltimore-18, Maryland, U. S. A.

This periodical is issued monthly. Two volumes a year are issued, each consisting of approximately 400 pages, and beginning in January and July, respectively.

Subscription price. In the United States and its possessions $6.00 per year. In Canada $6.25 per year; in foreign countries $6.50 per year. Prices for back volumes and back single numbers on application. Single numbers of the current volume, when available, $.75. Prices are net, postpaid.

New subscriptions and renewals are entered to begin with the first issue of the current volume. Should any issue of the current volume be out of print at the time the subscription order is received, the pro rata value of such numbers will be credited to the next volume, and the renewal invoice therefor adjusted accordingly.

Subscriptions should be renewed promptly. To avoid a break in your series, subscriptions should be renewed promptly. The publisher cannot guarantee to supply back issues on belated renewals.

Subscriptions, new or renewal, may be sent to the Publishers or ordered through your agent.

Subscriptions in the British Empire except Canada may be sent to: Baillière, Tindall & Cox, 8 Henrietta St., Covent Garden, London, W.C. 2.

THE JOHNS HOPKINS PRESS
BALTIMORE-18, MARYLAND, U. S. A.

Entered as second-class matter at the Baltimore, Md., Postoffice. Acceptance for mailing at special rate of postage provided for in Section 1103, act of October 3, 1917. Authorized on July 3, 1918.

"RIGHTS, HONORS AND PRIVILEGES THERETO APPERTAINING"[1]

ALAN M. CHESNEY

Members of the Graduating Class,

Ladies and Gentlemen:

You are participating, this morning, in what is, for the School of Medicine, an unusual ceremony. This is the first time, so far as I am aware, that separate graduation exercises have been held by the School for its graduates. In the past the candidates for the degree of Doctor of Medicine have received their degrees at the regular commencement exercises of the University, in which the other divisions of the institution participated, but since the School of Medicine is now operating under a different calendar from that of the other University divisions, it has not been possible to arrange joint commencement exercises this year. Let me assure you graduates at once, however, that this fact will have no bearing upon the validity of your diploma. The value of that instrument, which is about to be awarded to you, happily rests upon far firmer foundations, not the least of which are a tradition and a performance that now date back a full half-century. In view of the fact that we are about to close the academic year which marks the semicentennial of the opening of the School of Medicine, it seems to me essential that we pause for a moment and pay a tribute of respect to the individuals who were responsible for founding the institution and for launching it upon its thus far successful career. To those individuals we owe a great debt of gratitude, and we would indeed be guilty of gross filial impiety if we did not, at least once in every fifty years, make public acknowledgment of that debt.

First of all among those persons must be mentioned that wise old Quaker gentleman, Mr. Johns Hopkins, whose broad vision and generous means made possible this University and this Hospital, which have meant so much to Baltimore, and, I make so bold as to assert, to

[1] An address delivered at the Graduation Exercises of the School of Medicine of the Johns Hopkins University held in Hurd Memorial Hall of the Johns Hopkins Hospital, August 18, 1944, at 11 A.M.

this nation as well. Next comes that fine group of Trustees to whom he entrusted the carrying out of his twin enterprises, of whom Mr. Francis T. King, the first President of the Hospital Board and also a member of the Society of Friends, was the outstanding figure. We must also mention that able man upon whom they called for advice, John Shaw Billings, of the United States Army, himself a physician and an extremely wise counselor, and Daniel Coit Gilman, the first President of the University, who had such a clear vision of what the School of Medicine should be and worked so faithfully to make that vision a living reality. Nor should we forget to mention, of course, that unusual group of women headed by Miss Mary Elizabeth Garrett, who, when the outlook seemed very dark indeed, came forward with the material means which ensured the opening of the School. To these founding fathers—and mothers, I should add, we acknowledge our debt this morning.

But these are by no means all to whom you and I are beholden. I would also cite that extraordinary first Medical Faculty that had the responsibility of actually making the new enterprise work. Theirs was the task of determining the plane on which the new institution should operate, of establishing its ideals and its tone, and it is to their everlasting credit and to our great good, that they succeeded as handsomely as they did. Let no graduate of this School ever forget the names of Gilman, Welch, Osler, Halsted, Kelly, Hurd, Mall, Abel and Howell, for no matter what the year of his graduation, and no matter whether he ever saw them in the flesh or not, the fact is that the value of the diploma which he holds is conditioned by the very fact that those men once lived and carried out an experiment which, so far as I know, is altogether unique in medical education.

However, that first Faculty group is not alone responsible for the value which attaches to the diploma which you receive to-day, and I am sure that the members of that group would be the last to put forward such a claim although I think that perhaps they deserve the lion's share of the credit. Others in the Medical Faculty who followed in their footsteps and unhappily are no longer with us, must be accorded their full measure of recognition, as well as the many benefactors who through their generous gifts to the Hospital and to the School of Medicine have made possible the material growth and development of these two institutions to the point where they stand to-day.

And there is still another group of persons whose labors have contributed in no small measure to the value of your degree, and we must not fail to include them on our honor roll. I refer to the long list of graduates of this School who by their excellent work in the practice of medicine, in research, and in teaching, have added lustre to the name of the institution. They too, by the manner in which they have carried on their daily work, have helped to make the School's degree a thing of value,—"worth its face in the currency in the world," to use Gilman's own words.

So we see, ladies and gentlemen of the graduating class, that the thoughts and the labor of many men and women over the past half-century have combined to determine the face value of your diploma and to make it, I think I may say, one of which you have every right to be proud. May I remind you that you will always have a considerable stake in that diploma, and may I call your attention to the fact that from now on you too will have the opportunity to do your share in maintaining and enhancing the value of this School's degree? I trust that each one of you will not fail to add a measure of distinction to it.

It is pertinent at this point to inquire just what your new-won diploma means. According to the traditional phrase used in these graduation ceremonies, its bestowal admits you to certain unnamed "rights, honors and privileges." What are those rights? Primary among them is the right to call yourselves doctors of medicine. But what is a doctor of medicine? The public in general thinks of a doctor of medicine as one who knows all about the ills of the human body and how to treat them. Between ourselves, you and I know how far wrong the public is in that conception, even if we choose not to broadcast that fact. The word doctor, as you know, is derived from the Latin verb, docere, which means to teach, and the title "doctor" in the medieval universities implied that its possessor was so well versed in a given field of knowledge that he was qualified to teach in that domain. How many of you would merit the title on that basis? I shall not try to frame a definition for the title this morning, however—rather shall I endeavor to describe your present qualifications and express a hope.

First of all you have had the good fortune to be born with sufficient intelligence to acquire what is generally spoken of as a liberal education, with emphasis on the natural sciences; in other words, the fairy godmother who presided over the matching of the genes which were

to determine your future development as individuals was good to you, —better, I venture to say, than to many others of your species. Moreover your lines have fallen in pleasant places, economically speaking, for circumstances have combined to enable you to obtain both a general education and a professional education largely through the material aid of others, a boon which has been denied many other members of your generation. In addition to the time spent in acquiring your liberal education you have devoted four academic years to studying medicine. That means that you have acquired more or less familiarity with the complex structure and function of the human body, and with the behavior of the individual who inhabits that body. You know something of how that body reacts to injurious agents, and how the individual's behavior is influenced by forces over which he may or may not have control. You have acquired a modicum of skill in analyzing the manner and extent of the body's reaction to injurious agents, and also, I trust, a modicum of skill in analyzing the behavior of an individual under adverse influences. Finally, you have attained to some knowledge of how to aid the body in its reaction to noxious agents, and how to help the individual human being meet the problems, both personal and social, that are posed by his illness. It is this sum of knowledge plus skill that gives you the right to call yourselves doctors of medicine, but I would deny you that right did you not possess one further bit of knowledge, to wit, the realization that your ignorance of the human being far exceeds your knowledge of him. This statement is not meant in any personal sense, of course. It is merely a recognition of the fact, to which I am sure you will all subscribe, that while medicine to-day covers a vast domain of knowledge there is still much unconquered territory that is to be gained only by continuous study. You have been students of medicine with us for four college years—if we of the Faculty have not made you students for the remainder of your natural lives we have indeed failed in our task, for the true conception of a doctor of medicine, to my way of thinking, is that of a person learned in his profession, but cognizant always of the limitations of his knowledge and ever desirous of pushing the boundaries of that knowledge farther and farther into the unknown. This, then, as I see it, is the "right" to which the degree of Doctor of Medicine admits you—the right to be always a student in your chosen

field, and I venture to express the hope that each one of this class will always exercise that right to the limit of his ability.

But what is the "honor" to which the degree of Doctor of Medicine admits you? I claim it to be that of membership in an ancient and worthy guild, a company of men and women whose main business all down the centuries has been the conquest of disease and the alleviation of human ills. There are great names in that company! Is it not an honor to be one of a guild that has numbered among its members Hippocrates, Galen, Harvey, Paré, Sydenham, Hunter, Pasteur, Koch, Ehrlich, and a host of others far too many to mention by name? Is it not an honor to belong to a profession which, in spite of all that has been recently said about it by its critics is, I submit, composed by and large of unselfish men and women? I know that there have been and are self-seeking persons in our profession, doctors who are more interested in what they will get out of the patient than what they will give, who do not scruple to charge all that the traffic will bear and even more, but it is my considered judgment that they are in the minority and I know that such persons are not respected by the majority of their fellows. Certainly their departure from the high tradition of the medical profession, the tradition that says a physician shall not ask himself "can this patient pay?" before he gives his services, is more than offset by the great numbers in the profession who have given their services unselfishly and without stint, never stopping to consider whether or not the patient could or would ever pay for those services. It is my hope that the members of this class will always adhere to this ancient tradition of the medical profession and will regard medicine as a calling and not solely as a means of gaining a livelihood or of obtaining wealth. Unless the members of the medical profession, to which you now belong, cleave to that ancient conception of the profession, they will forfeit the confidence of the people which they have enjoyed by and large up to this time, and the people will then take matters into their own hands, with what results one hesitates to contemplate.

So much for the honor which attaches to your new-won degree. What of the privileges? Your main privilege will be to deal with the most precious commodity in the world—human life. Nothing is of so much value as the life of a human being. It may seem odd to make

that assertion when so many persons are formally engaged in destroying just that thing, but the fact remains that life *is* of transcendent value to the individual even though on occasion he is willing to give it up for others, but it is precisely this willingness to surrender it on occasion for the benefit of others which makes it of such enduring value. Is it not a privilege, then, to be vouchsafed the knowledge of how to preserve the most valuable thing in the world, even if only to a limited extent? And if you do not yet possess the requisite knowledge to preserve human life under all occasions because the knowledge of your craft is itself limited, is it not a privilege to be able at least to dispel pain and bring comfort in the face of a relentless disease process that will not be brooked of its victim? Is it not a privilege to be taken into the deepest confidence of another human being who is tortured by fears, obsessions, delusions even, and by showing your manifest interest in him, and by exercising such patience as you have and such power of reasoning and persuasion as you can summon up, dispel those same fears, obsessions and delusions and turn night into day for that particular person? Is it not a privilege to be able to study the phenomena of disease, to try to make your own contribution toward pushing the boundaries of medical knowledge just a little farther back into the unknown?

I hope that you will agree with me that these are indeed great privileges to which the degree of Doctor of Medicine admits you, but it is a truism that privileges carry with them responsibilities, and you who are now set apart from the generality of mankind because of a preferred position in society, have a direct responsibility toward that society of which you are a member. That responsibility, briefly stated, is the trusteeship of the health of your fellow citizens, both as individuals and as a group. You may not always find it easy to discharge the obligations of that trusteeship, not only in the handling of individual case problems that arise in the course of the day's work, but more especially in the solution of the manifold problems of medical care that are presented by a complex industrial civilization such as ours has come to be. In this latter connection you will be beset by loud clamor at times, you will be confronted with apparently selfish or stupid acts by misguided members of our own profession, I regret to say, you will be approached by advocates of this or that form of organization of medical practice, some of whom are so naive as to suppose that the task of providing good medical care for everyone

is solely a matter of organization quite apart from the level of intelligence and the ethical sense of the men and women who must carry on the real business of supplying medical care—the men and women behind the stethoscope and the scalpel—the ultimate doctors who have to do the day's medical work.

All these multifarious questions will crowd in upon you at times and may perhaps confuse you. If you are unduly beset by them there is one thought that may be of assistance, one test which you may apply to every proposal that is brought forward whether it concerns the individual or the group. Indeed, I think I may call it the acid test, or the indicator by which the acidity or alkalinity of the solution is to be judged. That test consists in simply applying to every proposal the question—Does the arrangement which is suggested really serve the interest of the patient? Is it for his or her good? It is your responsibility to apply that test fairly and critically, not only to the problems posed by the individual patient who is under your supervision, but also to the proposals that are put forward in regard to the provision of medical care for the group of which you are a member. If you will judge such proposals not by the effect they will have upon your own pocket book, or your own leisure, but solely by the effect which they will have on the welfare of your patients, you will deserve to be a member of the medical profession and will, I believe, be happier in your chosen career.

These, then, ladies and gentlemen of the graduating class, are the rights, honors and privileges which it seems to me belong to the degree of Doctor of Medicine, but I would be ungenerous indeed if I did not, in conclusion, say something of your achievements in obtaining that degree. After all, it is not such an easy thing to come by, and certainly no one within these walls would have the temerity to maintain that the members of the Faculty had gone out of their way to feed you with a spoon. May I remind you that when I had the honor to address you for the first time on the occasion of your matriculation into the School of Medicine I gave you fair warning that you would be thrown largely upon your own resources and that the going might be rough at times? I doubt not that such has been the case, but the American youth is a hardy animal and enough of you have survived the journey and come safely through. Because of that fact may I, on behalf of the Medical Faculty, congratulate you and wish you well?

STUDIES ON FRACTURE CONVALESCENCE

I. Nitrogen Metabolism after Fracture and Skeletal Operations in Healthy Males

JOHN EAGER HOWARD, M.D., WILLIAM PARSON, M.D., KAY EISENBERG STEIN, HARRY EISENBERG AND VIRGINIA REIDT[1]

Two years ago a study of the metabolism and internal environment of patients who had suffered traumatic skeletal fractures was undertaken. It was hoped that light might be thrown on the factors which provoke the high incidence of urinary lithiasis and more rare renal complications(1), and also that, with a closer understanding of the metabolic processes during fracture recovery, therapeutic measures favoring optimal internal and external environment for the recovery of such patients might be disclosed. Since most fractures heal readily and without undue difficulties, the normal or usual pattern during convalescence was observed. Complications during fracture healing may be associated with deviations from this pattern.

Studies on the metabolism of convalescent fracture patients have been carried out by Cuthbertson and his colleagues in Glasgow (2). Large losses of body protein were observed. The source of this lost protein and the mechanism of the catabolism were discussed.

METHODS AND PROCEDURES

The present report deals with observations on the nitrogen metabolism of six patients following fractures of the large bones of the lower extremity, and includes comparative studies on three patients after operative procedures on the femur and one herniorrhaphy. Balance experiments were carried out on the metabolism ward of the Johns Hopkins Hospital, the orthopedic care of the patients being under the supervision of Dr. George Bennett and the orthopedic staff. The fracture cases studied were males, otherwise healthy,

[1] From the Department of Medicine of the Johns Hopkins University and the Johns Hopkins Hospital.

The work described in this paper was done under a contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and the Johns Hopkins University.

whose fractures healed satisfactorily in the opinion of the orthopedists. All patients were at bed rest in casts throughout the entire period of observation. Balance studies were begun so soon as the patients' general condition permitted accurate collections of urine and feces, which varied from 1 to 7 days after the trauma had been sustained. In the osteotomy cases it was possible to collect metabolic base line data preoperatively as well as to make observations immediately after the operation.

The methods of analysis and collection have been used for many years on the metabolism ward and are those which are currently in vogue.

Chemical determinations on urinary constituents were made, for the most part, from aliquots of collections covering 3-day periods. Voided urine was transferred directly to large bottles containing small amounts of concentrated hydrochloric acid and toluol.

Routine examinations were made on freshly voided specimens at weekly intervals for protein, sugar and microscopic constituents in the sediment. No abnormal findings occurred in these patients, nor was the non-protein nitrogen in the blood found elevated.

In the group of cases here reported, with a single exception, stool nitrogen is calculated as 10 percent of ingested nitrogen. In patient Fr., through 13 periods, each 3 days in length, the stool nitrogen was actually determined. Chart I shows the extraordinary parallelism between calculated and measured stool nitrogen in this patient. We thought that for the purpose of this study, in which we were dealing with quite large moieties, stool nitrogen calculations were of adequate accuracy for our purpose.

At weekly intervals blood was withdrawn under oil from brachial veins with minimal stasis for the following determinations: hematocrit, serum protein, calcium, inorganic phosphorus, chloride, bicarbonate, non-protein nitrogen, alkaline phosphatase and, in some instances, sodium and potassium content.

It was found impossible to obtain body weight determinations on these patients. Water was allowed ad libitum throughout, as was sodium chloride. The only drugs used were codeine and morphine for pain, cascara as a cathartic and, rarely, barbiturates as a sedative. Salicylates were scrupulously avoided. Various sulfonamide com-

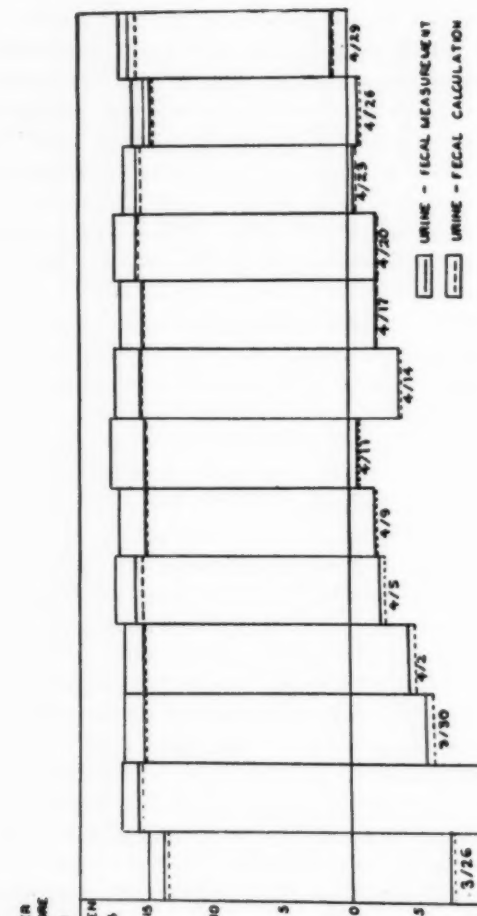


CHART I. The solid lines record measured fecal nitrogen, the dotted lines record calculated fecal nitrogen. Thus the top line is total ingested nitrogen, the next lower line is ingested nitrogen minus stool—dotted if calculated, solid if measured. Below the abscissa the negative nitrogen balance is portrayed. It may be seen that the actual measured stool nitrogen was always a trifle less than 10% of the ingested nitrogen value, with an average of about 8.5%.

pounds were used in the cases with compound fracture. Their dosage and periods of administration will be specifically recorded and discussed.

All temperatures were taken rectally. In the tables the recorded temperature is the average of the highest point reached each day during the 3-day periods.

Diets were formulated and served by members of the dietary department of the hospital under the personal supervision of Miss Virginia Reidt. The three diets used in this study are denoted in the charts and tables as S_0, S_0 and $S_{sub\ 0}$. Their nitrogen, caloric and calcium and phosphorus content are shown in Table I.

TABLE I

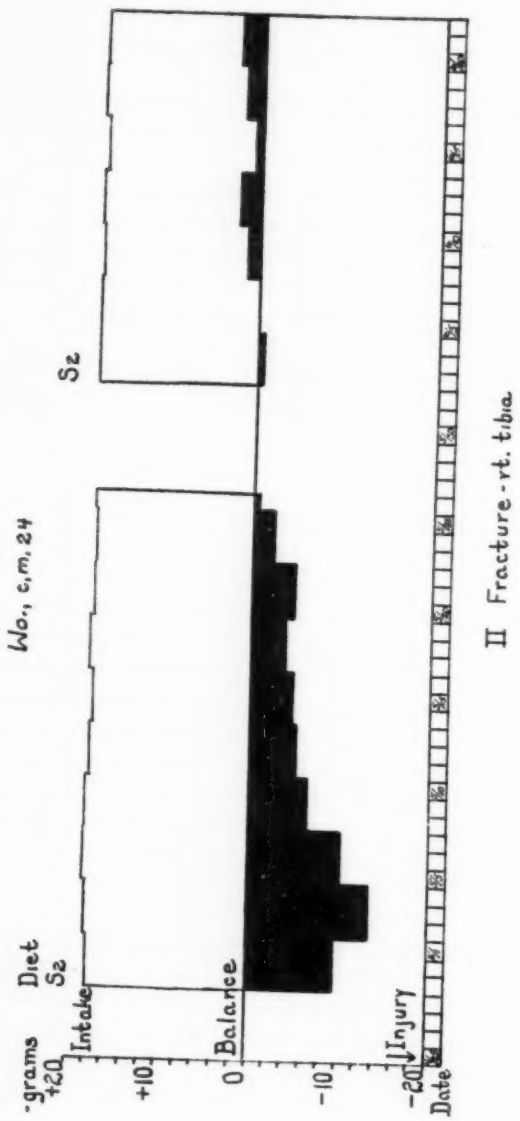
Key to diets

DIET	CALORIES	CALCIUM	PHOSPHORUS	NITROGEN
		gm.	gm.	gm.
S_0	Av. 1750 ±400	0.2 –0.3	0.8–1.0	Av. 11 ±2
S_{sub0}	Av. 1700 ±500	0.212–0.3	0.9–1.39	Av. 10.9 ±2.1
S_2	Av. 2610 ±400	2.0	2.1–2.5	Av. 17.3 ±2.5

Foods not eaten were saved and their constituents were calculated and administered in liquid form, so that only minimal variations in the desired intake of the elements under study were encountered. Nitrogen content of the diets was calculated from standard texts, and sample days were taken at random for analysis in our laboratory (3). The calculated and analyzed nitrogen content of the diets agreed, usually within 2%, always within 8%. Dietary, stool and urine nitrogen were determined by Kjeldahl method (4), the stool having been prepared by wet acid digestion (5).

RESULTS

All of the fracture cases showed losses of body protein of considerable magnitude. The nitrogen balance of a representative case is depicted in Chart II. Actual observed deficits averaged 190 gms. nitrogen. In one patient two 3-day periods are not included in the calculations because of errors in collection. Furthermore, metabolic studies were not begun until 3.3 days (average) after injury. In


N -grams
Diet
Sz
Intake
+20
+10
0
-10
-20
Balance
Injury
Date
Wo., c.m. 24
Sz
II Fracture - rt. tibia

this 3.3 day interval the patients consumed little or no food and were, from subsequent observations on other cases, of a surety in 10 or more grams nitrogen deficit per day. We feel justified, therefore,

TABLE II

Protein loss phase in fracture patients

PATIENT	AGE	DAY AFTER INJURY METABOLIC STUDY BEGUN	METABOLIC PERIODS	DIET	MAXIMUM NEG. N ATTAINED DAYS AFTER FRACTURE	DURATION NEG. N BALANCE	TOTAL N LOSS	FEVER AVERAGE
						da.	*gm.*	
Wo.	24-C	4	1–11	S_2	8th	31	179.7	101 in periods 1, 2 100 in periods 5, 7, 8 due to respiratory infection
Ha.	50-W	4	1–12	S_0	8th	39	187.5	100 in periods 1, 2, 3, 5, 6
Fr.	35-C	2	1–10	S_2	6th	31	124.2	101 in periods 1, 2, 3, 4 100.2–5 in periods 5, 6, 7, 8, 9
Ne.	57-C	7	1–14	S_0		50	130.8	101 in period 8—urinary tract infection
		(Periods 2–3 collections lost)						
Jo.	31-C	2	1–11	S_{sub0}	3rd	35	200.4	100.5 in period 2
Wa.	24-C	1	1–9	S_0	8th	28	257.1	100 in periods 1, 2 101 in periods 2, 3 100.5 in period 4 103 in periods 5, 6—abscess of leg
Aver. (Ne. omitted).....					6.6th	35.6	189.8	

Fractures: Wo.—right tibia; Ha.—right femur; Fr.—left tibia; Ne.—left femur; Jo.—compound of left tibia; Wa.—left femur (gunshot).

in stating that, in these six patients, the average loss of body nitrogen following fracture was more than 220 grams. Expressed in terms of protein, this would be about 1400 grams or, in terms of normal muscle protoplasm, 15 lbs. (7 kilos).

The peak of the observed nitrogen excretion did not occur in the

earlier specimens obtained but was manifested in the 3-day period which began 5.6 days (average) after injury.

For convenience we have divided our data into two phases, the first of protein loss, the second of protein repletion. We chose as an arbitrary dividing point the first 3-day period in which the daily output of nitrogen fell to within 1 gm. of the nitrogen intake. On this basis the duration of the phase of nitrogen loss in these patients averaged 35.6 days. Table II summarizes the over-all nitrogen

TABLE III

Repletion phase

CASE	PERIODS INC.	NO. OF DAYS FOLLOWED	TEMP.	DIET	TOTAL N LOST	TOTAL N REGAINED	% N REGAINED
					(gms.)	(gms.)	
Wo.	12–19	24	Normal	S_2	179.7	32.4	18
Ha.	13–16	12	Normal	S_2	187.5	0 (actually −5.4)	0
Fr.	Not followed				124.2		
Ne.	15–23	26	Normal	? (Prob. S_3)	106.2	0 (actually −8.7)	0
Jo.	12–31	59	Normal	S_2&S_3	200.4	27.9	14
Wa.	10–24	45	Normal	S_2&S_3	257.1	4.2	1.6

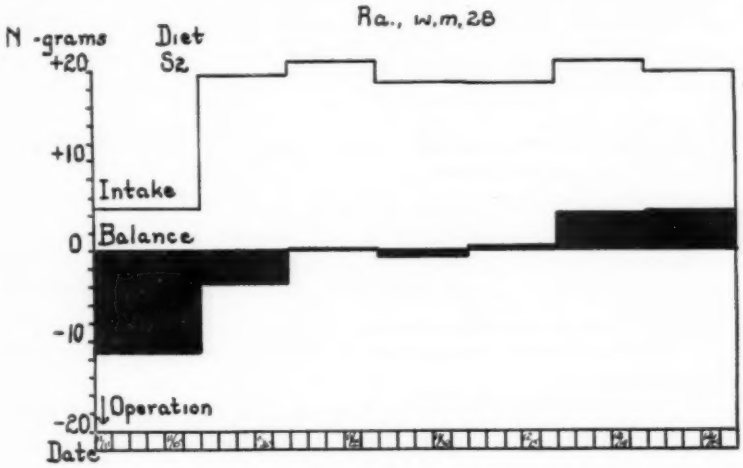
deficits in these six patients during the phase of protein loss, as well as showing the point of maximal excretion and the duration of the protein loss phase.

These observations on the magnitude of nitrogen losses, the delayed maximal excretion and the prolonged period of the negative nitrogen phase corroborate the data previously reported by Cuthbertson and his colleagues (2).

The study of the data in the repletion phase shows that these patients replenished their lost nitrogen at a very slow rate. Two cases, the studies on which lasted but 12 and 26 days respectively, after the nitrogen equilibrium had been approximated, actually showed

further slight deficits (Ha. and Ne.). The other three, who were followed for 24, 59 and 45 days respectively, regained only 32, 28 and 4 grams of nitrogen. This constitutes a restoration of but 18%, 14% and 1.6% of the losses sustained. Table III summarizes the pertinent data in the repletion phase during which these cases were followed.

Nitrogen metabolism data were obtained on four patients subsequent to operative procedures. Three operations involved the



III - Osteotomy - l. femur

skeletal system; one was a simple herniorrhaphy. The nitrogen balance in a representative case is depicted in Chart III. It was found that nitrogen losses were of much smaller magnitude than in the traumatic fracture cases and of briefer duration. The peak of nitrogen deficit was again delayed, appearing on the fourth day (average) after operation. The patients with skeletal operations were also well nourished, vigorous young males. The herniorrhaphy was performed on one of our fracture patients at the end of his nitrogen depletion phase, after there had been a loss of 200 gms. in the month subsequent to his injury. There were no instances of infec-

TABLE IV

Nitrogen depletion phase after operations

PATIENT	AGE	DATE, TYPE OF OPERATION	DIET	MAXIMUM NEG. N ATTAINED (DAY AFTER OP.)	DURATION NEG. N PHASE	TOTAL N LOSS
					days	*gms.*
Wh. Op. 1	16	12/24/42; manipulation hip; gas, ether	S_0	2nd	9	28.8
Wh. Op. 2		1/11/43; subtrochanteric osteotomy; sod. pentothal, ether	S_0*	5th	11	26.8
Wo.	24	5/27/43; hernia repair; procaine	S_2*	3rd	6	42.2
Je.	16	11/11/43; subtrochanteric osteotomy	S_2**	4th	11	86.2
Ch.	21	12/13/43; subtrochanteric osteotomy	S_2***	6th	10+ (still in neg. bal. at end of study)	81.9
Average				4th	9 (Ch. omitted)	46.0 (Ch. omitted)

* Diet not entirely consumed in first 5 days after operation.

** Diet not entirely consumed in first 6 days after operation; diet supplemented in last 4 days.

*** Diet supplemented in last 2 days.

TABLE V

Nitrogen repletion phase for operative cases

PATIENT	PERIODS INC.	NO. OF DAYS FOLLOWED	TEMP.	DIET	TOTAL N LOST DURING DEPLETION PHASE	TOTAL N REGAINED DURING REPLETION	% N REGAINED
					gms.		
Wh. Postop.	10–12* 13–37*	9 / 75 } 84	N	S_0 S_2	26.8	−0.3 / 216.3 } 216	807
Wo.	12–19*	24	N	S_2	42.2	32.4	77
Je.	3–10†	42	N	S_2 + amigen per. 8–10	86.2	149.5	174

* 3-day periods.

† 5-day periods except 8 & 10 which were 6 days.

tion in this group. One patient had no fever; one had ½ degree for one day; one had ½ degree for three days and one had ½ degree for six days. Table IV summarizes the data during the protein loss phases of these patients.

Again in sharp contrast to the fracture cases, the operative patients were found to restore their nitrogen losses quite rapidly. Table V records pertinent data in this regard during periods in which we were able to follow these patients. The postoperative period after Wh.'s first operation was of but 8 days' duration after nitrogen equilibrium had been established and is, therefore, not included in the chart.

DISCUSSION

Nitrogen losses of a magnitude sustained by our fracture patients are probably of considerable importance to the body economy and must not be overlooked in designing therapeutic measures. Other types of trauma are also associated with losses of body nitrogen (6). Factors which might conceivably play a role in these nitrogen losses are: disuse, anesthesia, sulfonamide compounds, fever and infection. These will be briefly discussed. A more detailed discussion of the part played by diet will appear in a subsequent paper.

Disuse atrophy. It is common knowledge that exercise of a part results in muscle hypertrophy and, conversely, disuse results in tissue atrophy. When a limb is removed from a cast after a long period of immobilization, the wasted tissues appear in sharp contrast to the good limb. It is obvious, therefore, that nitrogen is lost from the immobilized limb, be it to the exterior or to some other part of the organism. It is believed, however, that the protein losses herein discussed are, in but small part, accounted for by disuse. For the factor of disuse was equally present in the osteotomy cases, with similar areas immobilized under identical environmental conditions; yet the total nitrogen losses exhibited by the fracture patients greatly exceeded those in the operative cases. There may have been more atrophy in the fractured limbs than in the operative cases after cast removal (although this was not discernible) but, if so, other factors than disuse must be called on to account for it. Furthermore, the factor of simple bed rest alone will not account for nitrogen losses of

this magnitude; as a matter of fact, the operated patients were studied under similar physical circumstances, except for the casts, before operation and were found to be in nitrogen equilibrium.

Anesthesia. There appears to be little or no relationship between the type of anesthesia employed and the over-all nitrogen losses exhibited in this group of patients. All of the osteotomies were performed under general anesthesia (3 under sodium pentothal and ether and 1 under nitrous oxide and ether). The fractures were set and manipulated in only one instance under general anesthesia. It was our impression that the major effect of anesthetic agents was on the appetite and ability of the patients to take their food—a fact which will be discussed anon.

Fever and infection. All the fracture patients had fever for varying periods of time, but in only one instance did this rise above 101°. The evaluation of the role played by fever in the nitrogen losses in these cases is not easy. Ne. had an elevation of 1.5° in period 8, due to an intercurrent urinary infection from which there was no effect on the intake of food. There was little appreciable effect on the nitrogen balance. However, Wa., whose fractured femur was caused by a bullet, developed an abscess of the soft parts two weeks after his injury, with fever of 103° for 6 days (despite sulfonamides) until the abscess had pointed and could be opened. A sharp fall in his nitrogen losses after the temperature fall coincident with the drainage could well be laid at the door of the toxic febrile reaction.

Since fever is accompanied by an increase in the general metabolism, it would seem obvious that processes associated with high fever would undoubtedly play significant roles in the general catabolic processes which would include protein catabolism. However, in the group here under discussion, where fevers were of minor degree, and in which there were many periods of high nitrogen loss without any fever whatever, our assessment is that the role played by fever in the protein losses was a small one.

Sulfonamides. Sulfonamide medications would conceivably affect nitrogen balance either by altering ingestion or absorption of foodstuffs or by affecting some change in the internal protein metabolism. As to absorption, Fr., whose stool nitrogen content was measured throughout, shows clearly that the sulfonamide had no de-

tectable effect on the absorption of nitrogenous elements. In none of the group of four compound fractures did sulfonamides cause nausea or anorexia which interfered with their prescribed dietary intake. In each instance, where other factors were not obviously active, the period after cessation of the sulfonamide showed a small decrease in nitrogen losses (and total balance) as compared with the preceding one. The infection for which the drug had been given had, of course, cleared, too; and we are unable, therefore, to denote any definite effect on the nitrogen metabolism in these cases to sulfonamides per se.

Food intake. The relation between the magnitude of body protein losses and the caloric and protein content of the diets fed such patients is naturally of much interest. A detailed discussion of such relationships in this group of patients forms the subject of another report. Suffice it to say here that *during their protein loss phases*, none of the patients felt inadequately fed; and those on the S_2 diet constantly had to be coaxed and cajoled to eat their full quota. It is not implied that the diets provided these patients were in any sense ideal; for the most part, however, they were above the normal standards for healthy adults, and we believe that they received, on an average, as much and as high quality food during their protein loss phases as is eaten by the average fracture patient treated at large in hospitals of this country today. It is our impression that the average healthy young male who suffers a major fracture today will suffer body protein losses of comparable magnitude to those presented in this communication. It has been found extraordinarily difficult to compel young vigorous patients of the type dealt with here to eat much food, especially during the height of their "catabolic" (or "protein loss") phase. In several instances we have attempted to give large diets by tube feeding and have met so much resistance to the tube *in this type of patient* that its use has been abandoned, because it was felt that the harmful effects far outweighed the possible advantages of higher diets thus provided.

SUMMARY AND CONCLUSIONS

Vigorous healthy male patients suffering skeletal fracture treated by ordinary methods sustain large losses of body nitrogen during the early phase of their convalescence. The catabolic nitrogen, which

is excreted in the urine, does not reach its maximum until 6 days after the injury is sustained; and nitrogen equilibrium is not reestablished for approximately 35 days. These observations confirm earlier reports by Cuthbertson. Under the circumstances of these experiments, repletion of the lost nitrogen was slow.

Non-fracture operative cases sustain comparatively much smaller and shorter nitrogen losses and repletion is more rapid and vigorous.

In agreement with Cuthbertson it is concluded that disuse atrophy, bed rest, anesthesia, fever and infection do not account for the major part of the nitrogen losses under discussion. Sulfonamide compounds did not appear to influence the over-all nitrogen metabolism in this group of patients.

BIBLIOGRAPHY

1. HOWARD, J. E., Ann. Int. Med. **16,** 176, 1942.
2. CUTHBERTSON, D. P., Biochem. J. **24,** 1244, 1930.
   CUTHBERTSON, D. P., Biochem. J. **25,** 236, 1931.
   CUTHBERTSON, D. P., Quart. J. Med. **1,** 233, 1932.
   CUTHBERTSON, D. P., Glasgow Med. J. **3,** 41, 1934.
   CUTHBERTSON, D. P., Brit. J. Surg. **23,** 505, 1936.
   CUTHBERTSON, D. P., MCGIRR, J. L., AND ROBERTSON, J. S. M., Quart. J. Exp. Physiol. **29,** 13, 1939.
   CUTHBERTSON, D. P., Lancet **1,** 433, 1942.
3. SHERMAN, H. C., Chemistry of food and nutrition, MacMillan, New York, 1941. Food and Beverage Analyses, Bridges, M. A., and Mattice, M. R., Lea and Febiger, Philadelphia, 1942.
4. CAMPBELL, W. R., HANNA, M. I., J. Biol. Chem. **119,** 1, 1937 (with modifications).
5. STEARNS, G., J. Lab. and Clin. Med. **14,** 954, 1929.
6. BROWNE, J. S. L., STEVENSON, J. A. F., AND SCHENKER, V., Minutes of the Conference on Metabolic Aspects of Convalescence Including Bone and Wound Healing, Third (March 12–13, 1943), Fourth (June 11–12, 1943), Fifth (October 8–9, 1943) and Sixth Meeting (February 11–12, 1944), privately printed by the Josiah Macy, Jr., Foundation.

INFESTATION OF THE GENITO-URINARY TRACT BY STRONGYLOIDES STERCORALIS: A CASE REPORT

RICHARD WHITEHILL, MAJOR, M.C., AUS AND
MITCHELL H. MILLER, CAPT., M.C., AUS

Strongyloides stercoralis is a human parasite whose usual habitat is the small intestine. We have recently encountered a patient in whom larvae of this worm were present in the urine. Because of the extreme rarity of this situation we thought it worthwhile to report the case.

CASE REPORT

A 22 year old, white, single sailor was admitted to a South Pacific base hospital on Apr. 17, 1944 because of frequency, nocturia and urgency. His past health had been good. For 3 years he had been troubled occasionally by lower abdominal discomfort after eating and relieved by the passage of gas by rectum. One year ago he had had an attack of sinusitis. He had lived in Illinois until joining the Navy 18 months ago. Since then he had been stationed in Michigan, Idaho, New Caledonia, New Hebrides and Fiji. He had been in the South Pacific area for about 10 months before this admission. The family history was noncontributory. It was impossible to date the onset of the present illness. As long as he could recall he had diurnal frequency up to 10 times. He had nocturnal enuresis until the age of 16. After the enuresis cleared he had nocturia of 2 times every night. Also for as long as he knew he had some urgency, most marked early in the morning. For 2 months the urgency was more severe and there was occasional incontinence in the early morning. One year ago a Navy doctor told him "something was wrong in 2 specimens of urine but the third specimen was all right." Five days before the admission here a routine urinalysis performed in this hospital showed a rhabditiform larva of Strongyloides stercoralis in the centrifuged sediment. The night before admission he had lower abdominal cramps and some diarrhea. He denied sodomy and pederasty, had had normal sexual intercourse once in his life and that 2 years ago. Physical examination on admission showed a well nourished and well developed white male.

His temperature was 100°F., pulse 96 and B.P. 120/80. The pupils reacted to light and accommodation. Hearing and vision were grossly normal. The nasal mucous membranes were mildly congested. The teeth were in good condition. The tonsils, throat and neck were normal. The thyroid gland was not remarkable. The chest was clear. The heart was normal. The abdomen was negative except that the colon was a little tender in each lower quadrant. The genitalia were normal. The joints were normal. The neurological examination was not remarkable. The dorsalis pedis and posterior tibial pulsations were strong. The peripheral arteries were soft. There was no lymph node enlargement. There was fungous infection of the feet and genito-crural regions and some excoriated prickly heat lesions on the legs. Laboratory studies were as follows: the hemoglobin was 17.9 gms., the white cell count 4,500, hematocrit 52%, icteric index 7, corrected sedimentation rate 19 mm. in 1 hour. The differential white cell count showed 44% neutrophils, 44% lymphocytes, 6% monocytes, 2% basophils and 4% stab forms. There were no eosinophils. Urinary sediments were examined daily during the period of hospitalization. Over the first 10 days rhabditiform larvae of Strongyloides stercoralis were observed on 4 occasions. Five cubic centimeters of one of these urine specimens were added to an equal quantity of normal stool. This stool had previously been negative for parasites and ova by careful examination using the zinc sulfate flotation method of concentration. The mixture was kept at 25–30° C. for 48 hours. At the end of that time microscopic examination of unconcentrated material revealed numerous rhabditiform larvae, ova and a small number of gravid females and adult male forms of Strongyloides stercoralis. These findings were confirmed by the parasitologist of a large British Colonial Service hospital. Occasional urines also showed a trace of albumen, a few white cells and granular casts. Urine cultures were sterile. Numerous stools were negative for Strongyloides but contained ova of Trichuris trichiura. A P.S.P. renal function test showed an excretion of 30% of the dye in 15 minutes and 75% in 2 hours. Complete urological examination was performed on April 19 and April 24 by Major Charles B. Brack. The external genitalia and prostate gland were normal. The prostatic fluid was normal. The urethra was normal. There was a small slightly trabeculated area on the posterior

bladder wall and a few small areas of injection in the mucosa. The trigone was slightly injected. The vesical orifice was slightly irregular with a small polyp-like projection at 2 o'clock. Both ureters were patent without obstruction to a #6 whistle tip catheter with small bulb. Retrograde pyelograms were normal. On the pyelogram films there was seen to be incomplete fusion of the transitional segment between the lumbar spine and sacrum, but no definite spina bifida. Cystometric study showed that the bladder held 300 cc. of fluid in 50 cc. increments at high pressure. There were no involuntary contraction waves. The readings were as follows:

Volume in cc.	*Pressure in cms. of water*
0	3
50	10
100	12
150	15
200	17
250	20
300	30

The voiding pressure was 60 cms. of water. Prostatic fluid, bladder urine and urine from each kidney were normal and contained no parasites. The urologic diagnosis was reduced bladder capacity with high pressures, cause undetermined.

Treatment of the Strongyloides infestation consisted of enteric coated capsules of gentian violet, 0.06 gram, by mouth after each meal from April 28 to May 12, 1944. After a week of this medication the symptoms of nocturia, urgency and incontinence cleared. Diurnal urinary frequency decreased to 6 times. Strongyloides also disappeared from the urine which was examined daily. The sediment of two 24 hour urine collections was negative and a mixture of each of these sediments with normal stool showed no parasites or ova after 48 hours. Urines, however, were never discoloured by the gentian violet. The Trichuris infestation was treated by hexylresorcinol 0.9 gram by mouth on April 27 and May 9, 1944. A stool specimen on May 6 was still positive for ova of Trichuris trichiura. The patient continued symptom free for the first time in many years. He was discharged to duty May 12, 1944. On May 19, 1944 he was symptom free. Urinalysis showed a specific gravity of 1.025, albumin negative and microscopic examination of the centrifuged sediment negative.

Urine mixed with normal stool contained no parasites after 48 hours. A stool specimen was negative for worms and ova. Cystoscopy and cystometric study were repeated by Major Brack on May 22, 1944. There was very slight trabeculation of the posterior bladder wall. The bladder mucosa appeared normal everywhere. The vesical orifice was slightly irregular but the polypoid projection described before was not seen. The posterior urethra and verumontanum were normal. The cystometric study was as follows:

Volume in cc.	*Pressure in cms. of water*
0	1
50	6
100	7
150	9
200	11
250	12
300	25

The voiding pressure was 60 cms. of water. The bladder held 400 cc. of fluid in 50 cc. increments at normal pressures. There were no involuntary contraction waves. The urologic diagnosis was normal bladder and normal cystometric study. Urine and stool specimens were both normal on May 22. On June 6, 1944 he was still free of symptoms except that he was voiding 6 to 8 times during the day. This may have been associated with the advent of cool weather at that time. Urine and stool specimens showed no parasites. Urine was also added to normal stool and the mixture kept at room temperature for 48 hours. At the end of this time no ova or parasites were demonstrated in the mixture.

DISCUSSION

We feel that the evidence here presented supports the diagnosis of infestation of the genito-urinary tract by Strongyloides stercoralis, a parasite ordinarily considered as an intestinal invader. Considerable care was taken in the collection of specimens to rule out the possibility of contamination of the collecting vessels. It is unfortunate that urine obtained by catheter failed to show the larvae, but their appearance in voided urine was inconstant. The parasite, however, was found in the urine on five separate occasions, and must have been an authentic inhabitant of the patient's genito-urinary tract. Our studies did not

determine the exact localization of the parasite. Fluid obtained from the prostate, bladder and both kidneys did not contain organisms. The only abnormalities encountered were revealed by examination of the bladder. The mucosa of that organ showed slight trabeculation, injection and one area of polypoid tissue. The cystometric readings demonstrated a reduced capacity with high pressures. All of these changes disappeared concomitantly with the disappearance of the patient's symptoms and of Strongyloides larvae from the urine. These facts suggest involvement of the bladder by the parasite.

We are also unable to explain the mode of infection of the genito-urinary tract, especially since Strongyloides was not found on repeated examination of stools. Although this worm is essentially one which invades the small intestine, cases have been reported in which it has been found in other sites. In their textbook, "Clinical Parasitology," Craig and Faust (1) cite articles by Ophüls (1929), Nolasco and Africa (1936), Torres and De Azevedo (1938) and Faust and De Groat (1940), in which were described instances of penetration of the bowel wall by Strongyloides larvae and their appearance in mesenteric venules, lymphatics, lymph nodes and the liver. In the texts by Craig and Faust (1), and Stitt and Strong (2), reference is made to the case of Fonara, who in 1923 reported hematuria in a woman in whose urine larvae of Strongyloides stercoralis were very numerous. In the limited bibliography at our disposal this is the only instance of occurrence of this parasite in the urinary tract that has been reported. It is of interest that our patient's symptoms were of such long duration. According to Craig and Faust (1), human intestinal strongyloidiasis has been observed to last for 15 or more years in the absence of reinfection. This lends credence to the history obtained from our patient.

The apparent therapeutic response of this patient to the oral administration of gentian violet is also interesting. According to Beckman (3), gentian violet was first proposed for the treatment of intestinal strongyloidiasis by De Langen in Java, and has been found to be quite efficacious in the hands of Faust and others. From a perusal of several authoritative texts on pharmacology we have been unable to gain information concerning the distribution and excretion of the drug when taken by mouth or injected intravenously. We have no direct evidence that it was excreted into the urinary tract of this pa-

tient. However, it seems of significance to us that following treatment by the oral route there was disappearance of the symptoms, signs and parasites and the apparent cure has continued for a month.

SUMMARY

Because of its extreme rarity we have presented a case of infestation of the genito-urinary tract by Strongyloides stercoralis. There is indirect evidence to suggest that cure was effected by the oral administration of gentian violet.

BIBLIOGRAPHY

(1) Craig, C. F., and Faust, E. C.: Clinical Parasitology, Ed. 2, Lea and Febiger, Philadelphia, 1940, pp. 249–259.
(2) Strong, Richard P.: Stitt's Diagnosis, Prevention and Treatment of Tropical Diseases, vol. II, Ed. 6, Blakiston, Philadelphia, 1942, pp. 1278–1286.
(3) Beckman, Harry: Treatment in General Practice, Ed. 4, Saunders, Philadelphia, 1942, p. 340.

THE UTILIZATION OF *d*-AMINO ACIDS BY MAN

I. TRYPTOPHANE, METHIONINE AND PHENYLALANINE[1]

ANTHONY A. ALBANESE

With the technical assistance of JANE E. FRANKSTON, VIRGINIA IRBY and DOROTHY L. WAGNER

From the Department of Pediatrics, The Johns Hopkins University and the Harriet Lane Home of the Johns Hopkins Hospital, Baltimore

The proposed use of mixtures of amino acids containing considerable amounts of racemic forms for parenteral (1, 2) and oral feeding (3) raises the question of the utilization and pharmacological action of the unnatural components of racemic amino acids in man. The use of the racemic forms is compelled by the circumstance that certain of the amino acids: methionine, isoleucine, valine, threonine, phenylalanine, and sometimes tryptophane and lysine can only be obtained in adequate quantities by syntheses which yield equimolar mixtures of the natural and unnatural forms. Although it is possible to resolve these products by chemical (4) or enzymic methods (5), the available procedures are laborious and impractical for large scale production.

Studies on the utilization of the optical isomers of a number of amino acids carried out on the rat and the mouse (Table I) have shown that in many respects these two species are alike in their ability to utilize some but not other *d*-amino acids. However, even these closely related species showed differences in behavior, the unnatural form of tryptophane being utilized readily by the rat and scarcely at all by the mouse and similar differences being apparent in the case of leucine. For this reason it is obviously unsafe to make assumptions about man on the basis of animal studies. Direct observations upon man are needed to determine which of the unnatural amino acids can be utilized and which not. We have attempted to elucidate this question by studying the excretion of the amino acids and their breakdown prod-

[1] The work described in this report was supported in part by grants from the Rockefeller Foundation and the Nutrition Foundation, Inc. Partial support was also derived from a contract recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and Johns Hopkins University.

ucts in urine after the administration of a test dose by mouth. This approach was first employed by Wohlgemuth (15) who found that when racemic tyrosine, leucine, aspartic or glutamic acid was fed to rabbits, the unnatural *d*-component appeared in the urine in a higher concentration than the natural isomer. A similar phenomenon was observed by Hirsch (16) when he fed racemic alanine to dogs. It is reasonable to assume that the unnatural component is more readily excreted because it is less readily utilized and removed from the blood; hence its concentration in the blood remains higher.

TABLE I

Utilization of optical isomers of the amino acids by the rat and mouse

AMINO ACIDS	RAT		MOUSE	
	l	*d*	*l*	*d*
Methionine	+	+ (6)	+	+ (12)
Phenylalanine	+	+ (7)	+	+ (12)
Tryptophane	+	+ (8)	+	± (12, 13)
Isoleucine	+	− (7)	+	− (12)
Leucine	+	± (14, 7)	+	− (12)
Lysine	+	− (9)	+	− (11)
Threonine	−	+ (10)	−	+ (12)
Valine	+	− (7)	+	− (12)

EXPERIMENTS WITH TRYPTOPHANE[2]

A comparison was made of the excretion of indole derivatives in the urine after the administration of *l*- and *dl*-tryptophane by mouth. These studies showed that although similar amounts of tryptophane and of indican were excreted in the urine under these conditions, the administration of *dl*-tryptophane gave rise in addition to an unknown metabolite that could not be detected when *l* (−) tryptophane was fed. This unknown metabolite reacted with iodine to give indigo red, and the quantity of indigo red so obtained accounted for nearly half of the *dl*-tryptophane ingested.

Four subjects were given 2.0 gm. (0.01 M) of *l* (−) or *dl*-tryptophane after an overnight fast. 240 cc. water were given with the amino acid

[2] These experiments are being reported in greater detail in another publication (19).

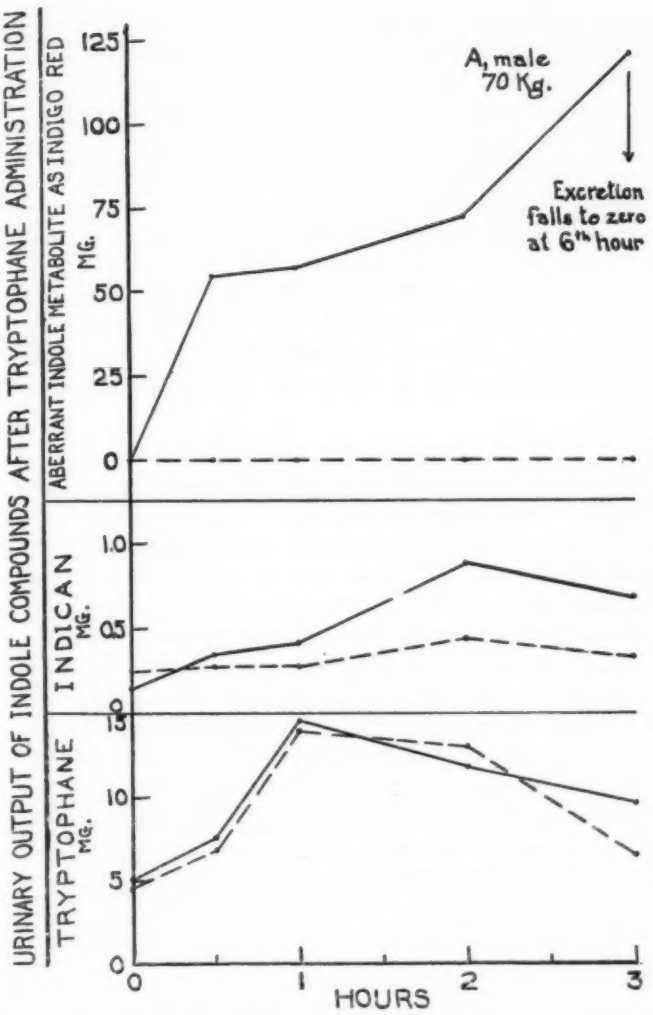


FIG. 1. Urinary output of some indole derivatives after administration of 0.01 M (2.0 gm) *l*- and *dl*-tryptophane. Solid line indicates excretion after ingestion of *dl*-form; broken line after ingestion of *l* or naturally occurring isomer.

and an additional 120 cc. at the end of the first and also at the end of the second hour in order to maintain uniform urine flow for the period of the experiment. Urine was collected at 0, ½, 1, 2 and 3 hours and analyzed immediately for tryptophane by the method of Albanese and Frankston (17), for indican by the Sharlit procedure (18) and for the unknown indole metabolite as described by us (19). Typical data shown in Fig. 1 reveal no significant differences in the excretion of tryptophane or indican, but show a marked excretion of the unknown metabolite after *dl*-tryptophane and none at all after *l* (−) tryptophane. Calculations indicate that the indigo red obtained from the unknown metabolite will account for 42 to 45 per cent of the ingested *dl*-tryptophane. Hence it is apparent that almost none of the *d*-component which gives rise to this product, is available for utilization by man.

EXPERIMENTS WITH METHIONINE

Observations were made on 4 human subjects who ingested 1.5 gm. (0.01 M) *dl*-methionine (Merck) or *l* (−) methionine.[3] The subjects were fasted overnight and given water as in the experiments on tryptophane described above. Collections of urine were made at similar intervals. The urine was analyzed for methionine by the titrimetric procedure described by us (20), for cystine by the Sullivan method (21) and for total and inorganic sulfur by gravimetric procedures (22). Representative data are shown in Fig. 2. It is to be noted that both forms of the amino acid induce a comparable temporary increase in the output of methionine. The cystine and total and inorganic S excretion likewise failed to show significant differences. In view of our experience with tryptophane it cannot be definitely concluded that the unnatural form of methionine is utilized, since it is possible that some abnormal metabolite of the *d*- form might have been present that was not detected. However, it is to be pointed out that the excretion curves of methionine and of the other metabolites which were studied failed to reveal such a difference.

EXPERIMENTS WITH PHENYLALANINE

Three subjects were fed 1.6 gm. (0.01 M) of *dl*-phenylalanine (Merck) or *l* (−) phenylalanine (Lemke). The conditions of administration,

[3] This material was kindly prepared for us by Hoffman-La Roche, Inc.

the water given and the urine collections were as described in the experiments on tryptophane and methionine. Phenylalanine was determined in the urine colorimetrically by a modification of the Kapeller-Adler method (23) described by us (24). The direct applicability of the method to urine was demonstrated by recovery tests and the fact that a 24 hour continuous ether extraction of acidulated urine for the

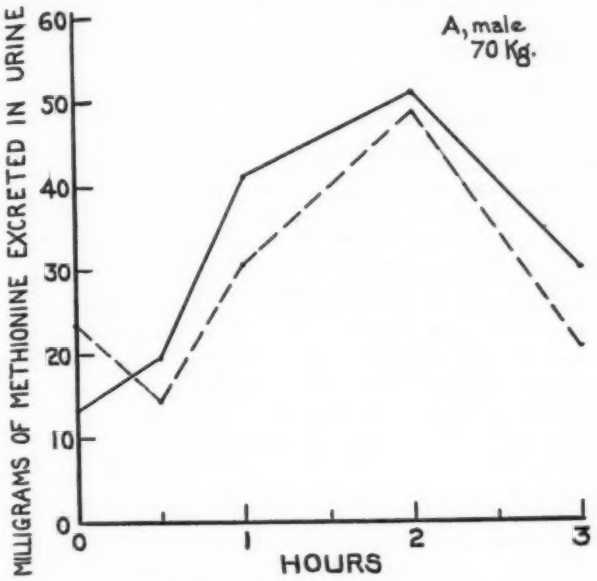


FIG. 2. Methionine excretion in the urine of fasting subject after administration of 0.01 M (1.5 gm) *l*- and *dl*-methionine. Solid line indicates excretion after ingestion of racemic form; broken line after ingestion of natural (*l*-) form.

removal of phenols failed to alter the phenylalanine value (Table II). 5 to 7 cc. samples of urine were found to yield colorimeter readings in the range of 1 mg. of phenylalanine standard. The free and total phenols were determined by the method of Marenzi (25). The results are shown graphically in Fig. 3. These indicate that approximately 25 per cent of the ingested amino acid is lost by excretion within 3 hours after the ingestion of the *dl*-phenylalanine whereas only 3 per cent or less is lost after feeding the natural form. The excretion of free and

total phenols failed to show significant variations. The striking loss of phenylalanine in the urine after the administration of the *dl*-form suggests strongly that the unnatural component is not readily utilized by man.

TABLE II

Recovery and extraction test data indicating applicability of modified Kapeller-Adler method (24) to estimation of phenylalanine in the urine

SPECIMEN	PHENYLALANINE FOUND MG.	PER CENT RECOVERY
5 cc. Urine A	0.50	
Same + 1.0 mg. *dl*-phenylalanine	1.47	94.0
10 cc. Urine B	0.88	
Same + 2.0 mg. *dl*-phenylalanine	2.90	102.0
10 cc. Urine C (1% HCl)	1.01	
Same after 24-hour continuous ether extraction	1.05	
5 cc. Urine D (5% HCl)	0.74	
Same after four 10 cc. ether extraction	0.78	

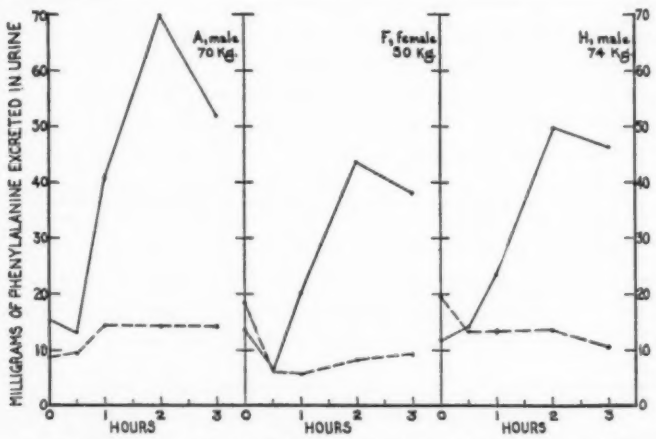


FIG. 3. Urinary output of phenylalanine in fasting subjects after administration of 0.01 M (1.6 gm) *l*- and *dl*-phenylalanine. Solid line indicates excretion after ingestion of *dl*-form; broken line after ingestion of *l* or naturally occurring variety.

The need of extending these studies to other amino acids, which are now available only in racemic form—particularly valine, isoleucine and threonine—has become obvious as a result of this work and is now engaging our attention.

COMMENT

The results reported indicate the desirability of studying the utilization of unnatural amino acids directly in man, rather than relying on inferences based on animal experiments. It is to be noted that in the case of tryptophane, man resembles the mouse rather than the rat in his lack of ability to utilize the unnatural form. In the case of phenylalanine the behavior of man is in sharp contrast to that observed in both the mouse and the rat.

The evidence obtained in this study that the unnatural forms of tryptophane and phenylalanine are not metabolized in man in the same way as the natural forms suggests the need for caution in the clinical use of preparations containing racemic amino acids. Until more is known of the fate and action of these unphysiological products it would seem preferable to rely on enzymic or acid protein hydrolysates which provide the amino acids in their natural form. Furthermore it is evident that the acid hydrolysates, in which destroyed tryptophane must be replaced, should be supplemented with *l* (−) rather than with *dl*-tryptophane.

The one virtue claimed for crystalline amino acid mixtures, as opposed to protein hydrolysates—more rapid administration—may prove to be one which is apparent rather than real, for it is possible that it is the greater amino acid loss in the urine that permits more rapid administration. That such losses are considerable when crystalline amino acids are given, is suggested by the work of Madden and his associates (2) who observed a rise in the excretion of undetermined N in their experiments*. It would seem logical therefore to establish the

* *Note added in proof.* Since this was written, a report by Cox and Mueller has come to our attention. These investigators made comparisons in dogs injected intravenously with a crystalline mixture (Vu) of ten essential amino acids and with an enzymic hydrolysate of casein (Amigen). When injected under similar conditions and at equal nitrogen levels, the urinary excretion of amino nitrogen was two to three times greater with the crystalline mixture.

merit of rapidly injected amino acid mixtures by careful studies of amino acid-N excretion.

SUMMARY

The utilization of the unnatural components of certain amino acids, now available only in racemic form, has been studied in man by measuring the urinary excretion of the particular amino acids and their derivatives.

Evidence is presented that the unnatural isomers of tryptophane and phenylalanine are not readily utilized by man. No evidence was found which indicated the non utilization of unnatural methionine.

The practical implications of these studies are discussed.

BIBLIOGRAPHY

1. Shohl, A. T., and Blackfan, K. D.: The intravenous administration of crystalline amino acids to infants. J. Nutr., **20:** 305 1940.
2. Bassett, S. H., Woods, R. R., Shull, F. W., and Madden, S. C.: Parenterally administered amino acids as a source of protein in man. N. England J. Med. **230:** 106, 1944.
3. Rose, W. C., Haines, W. J., and Johnson, J. E.: The rôle of the amino acids in human nutrition, J. Biol. Chem. **146:** 683, 1942.
   Rose, W. C., Haines, W. J., Johnson, J. E., and Warner, D. T.: Further experiments on the rôle of the amino acids in human nutrition, J. Biol. Chem. **148:** 457, 1943.
4. Fischer, E., *et al.*: Ueber die Spaltung einiger racemischer Aminosäuren in die optisch-aktiven Komponenten, I-V, Ber. d. deut. chem. Gesell., **32:** 2451, 1899; **32:** 3638, 1900; **33:** 2370, 2383, 1900; **34:** 3764, 1901.
5. Duschinsky, R., and Jeannerat, J.: Obtention des acides amines naturels à partir des recémiques à moyen de la *d*-amino-acide-oxydase., C. R. Acad. des Sciences. **208:** 1359, 1939.
6. Jackson, R. W., and Block, R. J.: The metabolism of cystine and methionine. J. Biol. Chem. **122:** 425, 1938.
7. Rose, W. C.: The nutritive significance of the amino acids and certain related compounds. Science, **86:** 298, 1937.
8. Berg, C. P., and Potgieter, M.: Tryptophane metabolism. II. The growth promoting ability of *dl*-tryptophane. J. Biol. Chem. **94:** 661, 1932.
9. Berg, C. P.: The availability of *d* (−) lysine for growth. J. Nutr. **12:** 671, 1936; compare with McGinty, D. A., Lewis, H. B., and Marvel, C. S.: Amino acid synthesis in the animal organism. J. Biol. Chem. **62:** 75, 1924–25.

10. WEST, H. D., AND CARTER, H. E.: Synthesis of α-amino-β-hydroxy-n-butyric acids. J. Biol. Chem., **122:** 611, 1938.
11. TOTTER, J. R., AND BERG, C. P.: The influence of optical isomerism on the utilization of tryptophane, histidine, and lysine for growth in the mouse. J. Biol. Chem., **127:** 375, 1939.
12. BAUER, C. D., AND BERG, C. P.: The amino acids required for growth in mice and the availability of their optical isomers. J. Nutr. **26:** 51, 1943.
13. KOTAKE, Y., ICHIHARA, K., AND NAKATA, H.: Ueber die Verschiedenheiten zwischen Ratten und Mausen ber Ernährung mit tryptophane und seinen Abkommlingen. Z. physiol. Chem. **243:** 353, 1936.
14. RATNER, S., SCHOENHEIMER, R., AND RITTENBERG, D.: Studies in protein metabolism. XIII. The metabolism and inversion of *d* (+) leucine studied with two isotopes. J. Biol. Chem. **134:** 653, 1940.
15. WOHLGEMUTH, J.: Ueber das Verhalten stereoisomerer Substanzen in thierischen Organismus, II Die inactiven Monoaminosäuren. Ber. de. deut. Chem. Gesell. **38:** 2064, 1905.
16. HIRSCH, R.: Ueber das Verhalten von Monoaminosäuren im hungerenden Organismus. Z. f. exp. Path. u. Ther. **1:** 141, 1905.
17. ALBANESE, A. A., AND FRANKSTON, J. E.: A new color test for tryptophane in protein hydrolysates. J. Biol. Chem., **144:** 563, 1942; also unpublished data.
18. SHARLIT, H.: A method for the quantitative estimation of indoxyl compounds in urine. J. Biol. Chem. **99:** 537, 1932.
19. ALBANESE, A. A., AND FRANKSTON, J. E.: A difference in the metabolism of *l*- and *dl*-tryptophane in the human. J. Biol. Chem. **155: 101, 1944.**
20. ALBANESE, A. A., FRANKSTON, J. E., AND IRBY, V.: The estimation of methionine in protein hydrolysates and human urine. J. Biol. Chem. *in press.*
21. SULLIVAN, M. X., AND HESS, W. C.: The determination of cystine in the urine. J. Biol. Chem. **116:** 221, 1936.
22. HAWK, P. B., AND BERGEIM, O.: Practical Physiological Chemistry, 11th Ed., pp. 760, 761. Blakiston, Philadelphia, 1937.
23. KAPELLER-ADLER, R.: Ueber eine neue Reaktion zur qualitativen und quantitativen Bestimmung des Phenylalanins. Biochem. Z. **252:** 185, 1932.
24. ALBANESE, A. A.: Colorimetric estimation of phenylalanine in some biological products. J. Biol. Chem. **155:** 291, 1944.
25. MARENZI, A. D.: La determination colorimétrique des phénols de l' urine. C. R. Soc. Biol. **107:** 734, 1931.
26. COX, W. M. JR. AND MUELLER, A. J. The relative efficiency of three forms of intravenously administered nitrogen on nitrogen balance and amino acid excretion. Presented before the Society for Pediatric Research, Atlantic City, Sept. 26, 1944.

NEPHRECTOMY FOR HYPERTENSION IN A 2½ YEAR OLD CHILD WITH APPARENT CURE FOR 3 YEARS

JAMES H. SEMANS 1ST LT., M.C., A.U.S.[1]

From the James Buchanan Brady Urological Institute and the Harriet Lane Home of the Johns Hopkins Hospital, Baltimore, Maryland

Some difficulty remains in selecting those patients with hypertension who can be permanently relieved by nephrectomy. The solution of this problem will be aided by reports of cases carefully studied before and after operation. In the case described below, the blood pressure changed from a maximum preoperative level of 200/134 to one of 98/62 at the time of the last visit, 3 years after operation. The microscopic diagnosis of the lesion in the extirpated kidney was chronic pyelonephritis. However, marked perirenal fibrosis, a cause of experimentally produced hypertension in dogs, seemed the most important etiological factor in this case. A retroperitoneal teratoma had been removed 4 months previously from the region of the kidney. Symptoms began following this operation.

CASE REPORT

D. E. M. (HLH #A20084), a male white child of 2½ years, was admitted for study at the Harriet Lane Home of the Johns Hopkins Hospital on April 23, 1941. The chief complaint was weakness and heart trouble, following an operation for the removal of a tumor 4 months previously.

History: The family history was noncontributory. The patient was born on October 27, 1938. Delivery was spontaneous and without event. The birth weight was 6 pounds and 3 ounces. The patient was fed by breast for 3 months and then put on a formula of carnation milk, karo syrup and water. This was supplemented by orange juice and cod liver oil. At 6 months he received cereals, vegetables and broth. The patient sat up at this time, walked at 1 year and talked in sentences at 2 years. He had had no serious illnesses. Before the present illness he had had no headaches. The vision was good, and

[1] This case report is based on observations made before the author entered active military service.

there had been no symptoms referable to the ears or throat. The teeth had appeared and developed on schedule. Blotches were noted on the skin after some foods were ingested, especially spinach.

Present Illness: At the age of 1½ years, exactly 12 months before admission, the patient began to walk. At this time it was noticed that his abdomen was abnormally large. Eight months later, December, 1940, he caught cold and began to vomit. Physical examination by the family physician showed a palpable tumor in the left upper quadrant.

The patient was admitted to Sibley Memorial Hospital, Washington, D. C., where the presence of the abdominal mass was confirmed. The heart and liver were not enlarged. No blood pressure reading was made. Study of the blood showed: hemoglobin, 68 per cent; red blood cells, 4.04 million per cubic millimeter; white blood cells, 10,600; differential count of leucocytes, polymorphonuclear neutrophiles, 30 per cent; lymphocytes, 61 per cent; monocytes, 6 per cent; eosinophiles, 3 per cent. Urinalysis: clear; acid reaction; no albumin, sugar, acetone or diacetic acid, erythrocytes, leucocytes or casts.

The tumor was removed on January 2, 1941, a little over three months before the present admission. Communication from Dr. Herbert S. Gates of Washington, D. C., revealed that at operation an ovoid tumor, the size of a grapefruit, was found on the left side of the abdomen in a retroperitoneal position. It extended across the midline, overlying the spleen, great vessels and both kidneys. Excepting pressure there was no apparent connection with these structures. The blood vessels supplying the tumor were very small. The spleen and left kidney were normal in appearance. Their surfaces were smooth.

Microscopic examination of the tumor showed several types of tissue. Some areas were acellular, consisting of collagenous fibrous tissue. There were large irregular islands of glial nerve and scattered patches of adipose tissue. The tumor was differentiated. Another section showed normal cartilage. In one area there was a definite line of ossification. The diagnosis was teratoma.

Following operation there was evidence of shock. A transfusion was given. No blood pressure was recorded. The patient was discharged from the hospital on the eighth postoperative day. Although no albuminuria was present before operation, urinalysis one month later showed albumin for the first time. There was also some increase in

urinary frequency. Nocturia occurred 5 or 6 times each night. There had never been any hematuria noted. The patient had no pain over his heart, but there was definite tachycardia and cardiac enlargement. The size and rate of the heart decreased satisfactorily. The liver was enlarged. There was no edema or cyanosis. Vomiting occurred several times a week, especially following activity. There was some

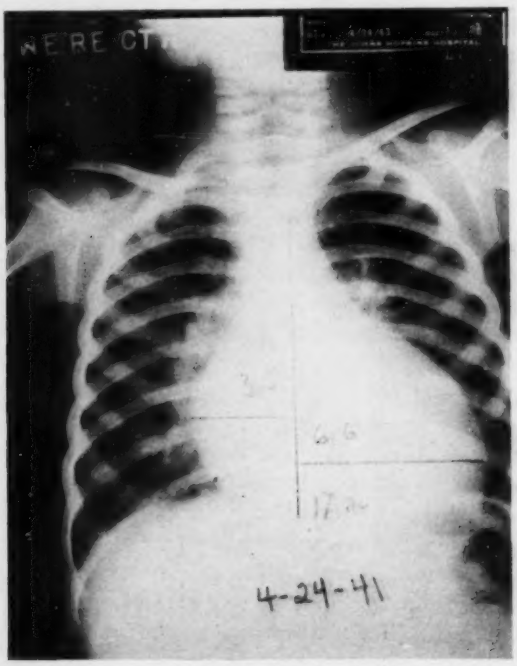


FIG. 1. X-ray of the chest, showing cardiac enlargement before operation

constipation, relieved by enemata. The appetite was good. The respirations were grunting for a long time, and this increased with exercise. The patient seemed well on some days, but was rather weak and listless on others. He was referred to the Harriet Lane Home for study.

Physical examination showed a pale white boy of 2½ years, who appeared chronically ill. The body weight was 45 pounds. The

arms and legs were thin. The abdomen was relatively large. The temperature was 37.3°C.; the pulse rate, 112 per minute; the respirations, 26 per minute; the blood pressure, 172/134 in the left arm. Examination a few days later revealed the blood pressure in the left arm to be 160/106. In the right arm it was 160/108; left leg 184/110; right leg 180/115. The color of the skin was normal. There was a long linear operative scar in the left upper quadrant which was well healed. There was no bony deformity. The pupils reacted well to light and accommodation. Ocular movements were normal. The eyegrounds, seen after dilatation with homatropine, were of good color and showed no papilledema. There was no retinal hemorrhage or exudate. The veins and arteries were essentially normal. Examination of the ears, teeth and throat was negative. There was no glandular enlargement. The heart was strikingly enlarged to percussion and by X-ray (fig. 1) there was precordial bulge. The pulsation was forceful. The point of maximum impulse was in the seventh interspace, 8 centimeters to the left of the midline. No thrills were felt. Examination of the abdomen showed the liver palpable 4 fingerbreadths below the costal margin in the right axillary line, as far as the umbilicus in the midline, and not palpable to the left of the midline. The edge of the liver was firm and sharp. The spleen and kidneys were not felt. The genitalia were those of a normal male of this age; both testes were descended. Neurological examination was negative. In summary, the positive findings were hypertension, cardiac enlargement and hepatomegaly.

Laboratory examinations: The Wassermann reaction was negative; hemoglobin, 16.8 grams or 116 per cent; red blood cells, 5.5 million per cubic millimeter; white blood cells, 14,560 per cubic millimeter; adult polymorphonuclear neutrophiles, 46 per cent; immature neutrophiles, 1 per cent; lymphocytes, 44 per cent; monocytes, 8 per cent; eosinophiles, 1 per cent; no basophiles or nucleated red blood cells. The blood platelets were numerous. There was moderate poikilocytosis and anisocytosis. Urinalysis: the voided urine was cloudy and straw colored; specific gravity, 1.012; reaction, alkaline; albumin, trace; no sugar, acetone or diacetic acid. In 14 specimens the albumin varied from 1 to 4 plus. There were 1 to 3 erythrocytes and an occasional hyaline cast per high power field. There were no leucocytes. Blood Chemistry: the serum non protein nitrogen was 32 milligrams per

cent; cholesterol, 177 milligrams per cent; Vandenbergh, normal. Blood serum chlorides were 100.7 milliequivalents; calcium, 10.6 milligrams per cent; phosphorus, 4.8 milligrams per cent; basic phosphatase, 9.9 Bodansky units; total proteins, 4.9 grams per cent; albumin, 3.7 grams per cent; globulin, 1.2 grams per cent; albumin/globulin ratio, 3. A phenolsulphonphthalein test on the voided urine showed 3 per cent excretion in the first half hour, 45 per cent in the second half hour, 25 per cent in the third half hour and 20 per cent in the final half hour, making a total of 93 per cent excretion at the end of 2 hours. The tuberculin test was negative to 0.1 milligram.

Cardiac measurements are shown in figure 1. The electrocardiogram on April 24, 1941 showed a normal sinus mechanism, sinus tachycardia, pathological T waves and a pathological ST_4 segment.

Urological studies: Intravenous pyelograms on 3 occasions showed no dye in the left kidney region. The right kidney was somewhat enlarged but otherwise, normal.

Cystoscopy on May 13, 1941 under drop ether anesthesia revealed a normal bladder and vesical neck. A No. 4 ureteral catheter passed through the right ureteral orifice to the renal pelvis. After using a whalebone probe it was possible to pass a No. 4 whistle tip catheter into the left renal pelvis. Neither catheter drained well enough for a satisfactory differential phenolsulphonphthalein test at this time. Two cubic centimeters of diodrast were injected under pressure into each renal pelvis, and bilateral retrograde pyelograms were made. Both kidneys were well visualized and were in normal position. The left kidney was definitely smaller than the right. The configuration of the pelvis on each side was normal. On May 28, 1941 Dr. Lloyd Lewis again passed a catheter up the left ureter. Only 5 cubic centimeters of urine and no phenolsulphonphthalein was recovered in two hours. Cultures of the urine from the bladder and from each kidney were sterile. Determination of the blood pressure on April 30, 1941 was 150/108 in the left arm; 154/120 in the right arm; 180/120 in the left leg; and 182/116 in the right leg. This followed a week's rest in bed. The highest systolic level noted was 200; and the highest diastolic level in the arms was 134.

In summary, there was no left pyelographic shadow after 3 separate injections, and a relatively small output of phenolsulphonphthalein

from the left ureteral catheter. From the above findings it seemed clear that the hypertension might well be caused by disease in the poorly functioning left kidney. The relationship of the recently removed teratoma to the diseased left kidney was not clear. It was decided that the severity of the hypertension and cardiac enlargement justified exploration of the left kidney.

Operation: June 2, 1941. Exploration and removal of left kidney (Dr. Semans). Under drop ether anesthesia a curvilinear incision was made in the left lumbar region and the left kidney exposed. There were many firm adhesions around the kidney and many small blood vessels in the perirenal fat. It was necessary to cut and ligate all of these before the renal pedicle could be exposed. Careful inspection revealed no constriction of the main renal vessels, which were small. The pedicle was divided and the kidney removed. Intravenous fluids were injected during the operation, followed by a small blood transfusion given on the ward. During the operative procedure the blood pressure rose within the first 15 minutes from 158/125 to 180/120. On return to the ward the blood pressure was 136/45. Six hours after operation the blood pressure was 145/80. The following day it was 160/80. The postoperative course was uneventful. A small Penrose drain was removed on the third postoperative day. The patient was discharged on the twenty-second postoperative day. The blood pressure remained fairly stable at 110/65 during the last week in the hospital.

Although albumin in the urine varied from a trace to 4 plus before operation, 2 analyses following nephrectomy showed no albumin. It was mentioned that the urine contained no albumin before removal of the teratoma.

Follow-up (2 weeks): When seen two weeks after discharge the parents said that the baby was greatly improved. He had become more active and no longer had gastrointestinal upsets. Examination showed that the blood pressure was 120/75. The urinalysis was negative. The heart was of normal size to percussion. The sounds were of good quality. Two months later the blood pressure was 100/72 on 2 determinations. The heart again was not enlarged to percussion. However, a sharp high pitched systolic murmur was heard at the apex. No abnormal masses were palpable in the abdomen, but the liver edge was

situated 2 fingerbreadths below the costal margin on the right side. Urinalysis showed the specific gravity to be 1.028. No albumin was present.

Follow-up (8½ months): When the patient was seen on February 16, 1942, 8 months following nephrectomy, the blood pressure was 102/68. He had grown 2 inches in height and gained 4½ pounds. A soft apical systolic murmur was heard in the heart. The liver edge was just palpable under the right costal margin. The urine was negative.

Follow-up (21 months): The blood pressure was 94/62. The patient weighed 36 pounds and was 39½ inches in height. His health had been excellent since his last visit. The heart was then of normal size in relationship with the chest. There were no adventitious sounds. The rate was normal. The incision was firm and well healed. A phenolsulphonphthalein test showed a normal appearance time of 5 minutes; 60 per cent of the dye was excreted in the first half hour and 8 per cent in the second half hour, a total of 74 per cent at the end of 2 hours.

Follow-up (3 years): The patient was last seen on May 23, 1944. The blood pressure was 98/62 in the left arm and 92/62 in the right arm. The urinalysis was still negative.

Pathology: Examination of the kidney removed at operation was made by Dr. Samuel Blackman of the Department of Pathology, Johns Hopkins Hospital. Externally there were several small vessels over the periphery of the kidney. These extended into the renal parenchyma, with branching in the region of the renal pelvis. There were three arteries and veins near the periphery of the pelvis, in addition to the main renal vessels.

The pelvis was very thick. The kidney was small. It measured 5.4 by 3.4 by 1.6 centimeters, and weighed 20 grams. This was about ½ normal weight for the kidney in a child of this age (1). The external surfaces were very irregular. There were rather large projecting smooth nodules which on section consisted of normal cortex and medulla. These areas alternated with numerous broad depressions. Sections through the depressed areas showed marked thinning of the tissue. In some places it was difficult to make out any of the normal architecture. The capsule was adherent and thickened.

Microscopic: Blocks were cut from twelve different areas of the kidney. There was evidence of chronic pyelonephritis in all the sec-

tions. There was marked chronic pyelitis. The submucosa was scarred and, in some places, vascularized. It was diffusely infiltrated with round cells. Some of the pyramids showed scarring and disappearance of collecting tubules.

Sections through the areas which looked normal in the gross showed normal architecture, patchy infiltration with round cells and relatively little change in the glomeruli and tubules. A few glomeruli, however, were hyaline. Also, there were some areas of tubular atrophy and superficial scarring.

The hilar branches of the renal artery were not sclerotic and there was no obvious change in the large intrarenal vessels. Throughout the sections the interlobular arteries were very prominent, and even the small branches had hypertrophied media. In addition, the small interlobular arteries in the areas of most marked chronic pyelonephritis showed considerable thickening of the intima.

Impression: Chronic pyelonephritis, left kidney.

DISCUSSION

The decision to explore the left kidney was based on several considerations. On three occasions intravenous injections of diodrast outlined only the right upper urinary tract. Failure to demonstrate secretion of radio opaque material by x-ray in any one instance is not pathognomonic of renal disease. But when one of two kidneys is persistently unable to secrete the material in sufficient concentration to cast a shadow, it signifies little or no function on the blank side. Also in this case, the left kidney secreted less phenolsulphonphthalein than the right.

At operation there was a large amount of dense scar tissue around the kidney. No constriction of either the renal artery or its extrarenal branches was evident. However, in view of the poor prognosis, and of the findings suggesting left renal disease, nephrectomy was carried out. The elimination of hypertension in this patient for a period of 3 years shows the relationship between the hypertension and the lesion in the left kidney.

While there was intimal thickening of some of the intrarenal arterioles, it seems probable that the perirenal fibrosis may have been a factor in producing this patient's hypertension and that previous removal of

the teratoma from the retroperitoneal space resulted in this fibrosis. In support of this role is the work of Page and Graef (2–4). These authors described hypertension in dogs, associated with experimental perinephritis. The phenomenon was produced by surrounding one kidney with cellophane. Marked perinephritis resulted. Hypertension persisting as long as 14 months disappeared after removal of the diseased kidney. Histologic study of the dog's kidney showed many zones of corticotubular atrophy and fibrosis. In the middle of one of the medullary pyramids there was a focus of polymorphonuclear leucocytic infiltration involving the interstitial tissue and the lumina of tubules. The blood vessels showed no intimal or medial changes. The glomeruli were well preserved. The renal artery and pelvis were imbedded in a dense mass of connective tissue containing leucocytic and histiocytic infiltration. Sections of other organs revealed no significant changes.

The experimental lesion just described is not unlike that in the present case. Both were associated with hypertension. Discussion of the mechanism of this phenomenon is not indicated in this report. The reader is referred to a review of the relevant literature by Abeshouse (5).

SUMMARY

1. A case of hypertension in a 2½ year old child with cure for 3 years following nephrectomy is presented.

2. The possible rôle played by perirenal fibrosis in the production of the hypertension is discussed.

REFERENCES

1. Mallory, F. B.: Pathological Technique, p. 377. Saunders, Philadelphia, 1938.
2. Page, I. H.: Production of persistent arterial hypertension by cellophane perinephritis. J. A. M. A. **113:** 2046, 1939.
3. Page, I. H.: Method for producing persistent hypertension by cellophane. Science, **89:** 273, 1939.
4. Graef, I., and Page, I. H.: Pathological anatomy of cellophane perinephritis. Am. J. Path. **16:** 211, 1940.
5. Abeshouse, B. S.: Hypertension and unilateral renal disease, review of literature and report of 16 cases. Part I, Surgery, **9:** 942, 1941. Part II, Surgery, **10:** 147, 1941.

BOOK REVIEWS

(These reviews represent the individual opinions of the reviewers and not necessarily those of the members of the Editorial Board of this Journal.)

Andreas Vesalius. A Bio-Bibliography. By Harvey Cushing. 229 pp. Illus. $15.00. Schuman's, New York, 1943.

Harvey Cushing was for more than forty years an ardent student and collector of everything relating to the great anatomist Vesalius. As John Fulton says in the preface to this book "In the impetuous Vesalius, Cushing saw a vigorous and indefatigable character with a stormy temperament similar to his own—a man with artistic leanings who gave unremitting attention to detail—all of which aroused Cushing's admiration and caused him to follow Vesalius with instinctive determination." For many years Dr. Cushing had planned to publish a Vesalius bibliography, and this idea finally developed into what he called a "bio-bibliography"—a book to reveal Vesalius in the time and circumstances that led up to the composition and publication of his several works. Dr. Cushing spent the last year of his life working on this task amid his great collection of Vesaliana, and when he died in October 1939 the projected book was about half written. It has been completed by a group of devoted friends led by John F. Fulton and W. W. Francis. Arturo Castiglioni, Edward C. Streeter, Mrs. John P. Peters and Miss Madeline Stanton have taken part also in this generous and useful labor. Mr. Carl P. Rollins as typographical adviser; Mr. Colish, the designer and printer; and Mr. Schuman, the publisher, have done for the book what Oporinus did for the Fabrica of Vesalius, making it a handsome as well as a learned work.

The book is primarily a bibliography of all the works published by Vesalius and by those contemporary anatomists and surgeons who learned from him or castigated or plagiarized him, and of books and articles about Vesalius. To this bibliography Dr. Cushing and the editors have added enough about the life of Vesalius to justify the "Bio-" part of the title; and in so doing, indeed, have brought the man to life, more than might be done in many a routinely biographical account. So much of the brief career of Vesalius as a scientist was devoted to the writing of his books, to planning for their illustration and publication, to exhortation of his publisher and to vexation over his plagiarists, that the story of his books almost becomes the story of his life. By this manner of telling it, many things are made clear that to the general reader, at least, have been obscure or matters of controversy. The question as to whether Calcar, the artist, does not deserve as much credit as Vesalius; the long history of the wood-blocks of the engravings, most of which are still in existence; the location of the countryside in the Euganean Hills shown as background in the plates of the Fabrica; the relations, often misunderstood, between Vesalius and Fallopius—these and many such matters, great and small, become vivid parts of the narrative of a great life. The post humous lore of Vesalius, too—the growth of his reputation through subsequent centuries;

the fate of the Fabrica, admired, influential, but seldom itself read and never translated; all sorts of learned gossip about Vesalian scholars and their plans, mostly abortive, to translate the Fabrica or otherwise to serve the Vesalian cause—is gathered here as in no other book.

The "Bio-Bibliography of Vesalius" is also, of course, a notable piece of Cushingiana. It would have been so even if Dr. Cushing had lived to complete and revise it, and it now frankly appears as a tribute to him as well as to Vesalius. Its personal flavor will be especially poignant to readers who had the good fortune to visit Dr. Cushing's Vesalian collection with the owner itself. Reading this book they can imagine themselves in his New Haven house, enjoying his enthusiasm and expert knowledge and listening to his mock embarrassment over the sums he paid for the rarest of his treasures.

With this personal charm there goes also, be it said in all respect, a certain pride of intellect not unfamiliar in the writings of rich and learned bibliophiles. Notwithstanding his modesty about his accomplishments in Latin and bibliography, Cushing was a real scholar, steeped in the history of Renaissance medicine, and he was not writing for beginners but for fellow-Vesalians. Here and there he assumes too much knowledge on the part of all but specialist readers, as in the matter, for example, of the insets in the plates of Charles Estienne, which should have had a paragraph of elementary explanation and a special illustration. People like Walther Ryff and Thomas Geminus pop onto the scene without such introductions, unnecessary of course to sophisticates, as might have made meeting with them easier for general readers. In short, these are not the first pages a beginner in medical history should read about Vesalius; but for those who seek admittance to the circle of complete Vesalians it is a *sine qua non*,—the only full-length work in English about Andreas Vesalius that is based on firsthand knowledge of his books and of contemporary medical history; a treasury of accurate bibliography; and withal a monument to the surgeon-scholar Harvey Cushing, a man after the heart of Vesalius himself.

G. W. C.

The Art and Science of Nutrition. By ESTELLE E. HAWLEY. 668 pp. Illus. $3.75. The Mosby, St. Louis, 1944.

This book presents a wealth of scientific knowledge of food and its uses. The authors have outlined the principles of normal nutrition and have indicated "when, why, and how the normal diet may be modified" to best treat disease and its metabolic consequences.

The book is designed primarily for teaching nurses, but because of its wide scope and up to date information, it would prove useful to anyone interested in nutrition and applied dietetics. Almost a quarter of it is devoted to lesson plans on the choice, preparation and serving of foods. The book uses visual education to good advantage as the one hundred and thirty-eight excellent illustrations attest.

This is a book which is well nigh irreplaceable in the library of the nurse or teacher of nurses, and of others of similar interests and training.

E. T.

A Surgeon's Fight to Rebuild Men. An Autobiography. By FRED H. ALBEE. 349 pp. Illus. $3.50. Dutton, New York, 1943.

Dr. Albee has had a full life. His delightfully written autobiography depicts a surgeon who attributes his success to early influences in life and whose life spans the active development of bone surgery into a longer field. Much has been contributed to the progress of Orthopedic Surgery by his ingenuity, skill, and experience in thousands of operations. During the past war he performed about half of the bone grafting operations.

Born on a Maine farm, he developed stamina and a rugged physique. His liking for surgery was born in an atmosphere of strict discipline and hard work. The principles of grafting trees suggested the principles of grafting bone. In his neighboring saw mill was conceived the idea of the Albee saw. As long as he could recall, his dreams were of medicine and particularly of surgery.

Through scholarships he was able to attend Harvard Medical School, where he received inspiration from Cabot, Putnam, Fitz, and Warren. Then to New York City, where he found his place in Orthopedic Surgery and gained national and international eminence. Toward the close of the last war, he conceived and developed United States General Hospital Number Three at Colonia, New Jersey, where he gained his richest experience, not only in reconstructive bone surgery but in physical therapy, the curative workshop, and the mental adjustment of soldiers to physical disability.

The book is interspersed with humor. While cases are frequently used to illustrate his development of the technique of surgery, there is no sense of textbook descriptions.

One is impressed with the vast energy of Dr. Albee and with his capacity for getting things done, even the prideful boast that he is a great fisherman. He journeys to Europe and to South America for lectures and operations, works in New York City and in his health center at Venice, Florida. Still he has time to write a charming account of his accomplishments.

R. E. L.

Treatment of Fractures. By GUY A. CALDWELL. 303 pp. Illus. $5.00. Hoeber, New York & London, 1943.

Dr. Caldwell has written very simply a textbook on the treatment of fractures. It is another valuable addition to the volumes on fractures published in recent years. It describes the methods of treatment proved by the author from a long experience. There is no effort to describe the process of the production of fractures but only the phase of treatment. Numerous line drawings are used for illustration of the text.

An excellent summary of the principles of reduction and the subsequent care of fractures in general emphasizes points that are most important. Then there is an analysis of each type of fracture. The author distinguishes between early treatment, late treatment, the handling of cases in the operating room and in the ward.

The modern treatment of compound fractures is adequately described; namely, the local treatment of the wound if handled six hours after injury or longer than six hours, the reduction of the fragments, chemotherapy, and the treatment of wound infections.

For fractures of the humerus, the author prefers the use of the hanging cast, with which he has had notable success, and for fractures of the humerus near the shoulder, often uses no fixation. There is an excellent summary of the treatment of fractures of the hip.

The textbook is short and concise, written in simple terms, and adequately illustrated. It is a good reference book for bone surgeons and for medical students.

R. E. L.

A Manual of Medical Parasitology. By CLAY G. HUFF. 88 pp. Illus. $1.50. The University of Chicago Press, Chicago, 1943.

This manual has manifestly been prepared primarily as an aid in class instruction, and it should prove valuable for this purpose. It is wide in its scope, including not only the important helminths and protozoa but also many of the arthropod vectors. The text is clearly written, and it is especially characterized by its conciseness and brevity. The reviewer feels that this feature has perhaps been carried too far, and that the book would have been improved by a moderate expansion of some of the topics.

A valuable feature is the inclusion of numerous keys and tables as well as illustrations (ten plates) to assist in identification of the parasites. These are often necessarily incomplete but will still be useful as an aid in teaching. There is an excellent colored plate illustrating the three important species of malarial parasites. There is also a chapter dealing briefly with the more important laboratory diagnostic procedures.

The book is not adequate as a reference book and is not designed as such. It should be valuable as a laboratory class manual for medical students and elementary courses in parasitology. Its appearance is timely in view of the increasing practical importance of the subject.

P. W. C.

Aesculapius in Latin America. By ARISTIDES MOLL. 1st Ed. 639 pp. Illustrated. $7.50. Saunders, Philadelphia, 1944.

The main purpose of this book, as the author attempted to express it in the preface, is to present every aspect of Latin American medicine in every historic period from pre-Columbian times up to the present day.

The author, in attempting to give unity to his discussion, describes Latin American medicine as a unity. Although Latin America can be considered as such in regard to language, history, and traditions, it is difficult to speak of medicine in these terms. This difficulty is manifest in several chapters where the accumulation of unconnected dates and names destroys the coherency of the presentation.

Nevertheless, the work of synthesis is admirable, and this is readily seen in the appendix where there are two chronological tables; one, medical and general, and the other arranged according to disease, each the fruit of intensive work.

There are a number of mistakes in the later chapters. For instance, the specialties of some contemporary doctors are incorrectly listed; and a very wide distribution is given for schistosomiasis, which has been found autochthonous only in Brazil, Venezuela, and Puerto Rico.

The bibliography is quite extensive.

We believe that the object of the book has been attained, and that it will be helpful to those who are interested in the history and current progress in medicine in the countries of South and Central America.

O. C. C.

Frontiers in Cytochemistry. Biological Symposia. Vol. 10. Edited by Professor NORMAN L. HOERR. Illus. 334 pp. $3.50. The Jaques Cattell Press, Lancaster, 1943.

It must be indeed gratifying to Professor Bensley to know that his efforts and counsel have been the source of inspiration to so many capable students who, as a token of gratitude, have honored the occasion of his 75th birthday with the series of lectures which constitute this symposium. These lectures present a timely discussion on recent advances of knowledge of the physical and chemical organization of the cytoplasm which have been achieved by the application of new concepts, methods and tools to the exploration of the ultimate unit of life—the cell.

The outstanding idea of these studies is the emphasis placed on the treatment of the cell, not as a biochemical unit, but as a composite and integrated function of each cytologic entity. Thus, it is pointed out that the individual chemical behavior of the cytoplasmic and nuclear bodies must be known in order that many of the difficulties of our current over-all concepts be adequately resolved.

Recent technological developments have given the cytochemist four new and important approaches to his problems: ultracentrifugation, electronmicroscopy, microdissection and microincineration. The use of the ultracentrifuge for the segregation and study of biocatalytic macromolecules is described by Stern. The value and application of this instrument in the investigations on distribution of cell nucleic acids and morphological constitution of the cytoplasm is discussed by Claude. Further application of this tool in the study of centrifugal force effects on cell topography is delineated by Beams. The ultrastructure of protoplasmic fibrils as disclosed by the electron microscope are ably set forth by Schmitt, Hall and Jakus. Studies on the effects of electrolytes on protoplasmic structures iso-

lated by microdissection are well presented by Chambers. The use of the micro-incineration and electron emission techniques for ascertaining the mineral distribution in the cytoplasm is reported by Scott.

Investigations and discussions of a number of cytochemical systems are also presented. The interrelationships of oxidation-reduction reaction systems to cellular respiration are thoroughly discussed by Barron. An insight to the complex chemistry of the fibrous nucleoproteins of chromatin is given by Mirsky and Pollister. The solubilities and isoelectric characteristics of liver cell globulins, mitochondria and nuclear chromatin isolated by cryogenic and saline extraction techniques are described by Hoerr. A discussion of the dynamics of the cell electrolytes is given by Lowry. Some phases of the general chemical structure of the cytoplasm are presented by Professor Bensley and Dr. Lazarow.

The practical implications of the preceding fundamental investigations to disease processes are also discussed. Most interesting are the observations presented by Cowdry on the cytological and histochemical changes induced by carcinogenic agents in epithelial cells of the mouse. Details of their investigations on the histochemical changes induced in rhesus motoneurons by root sectioning are discussed by Gersh and Bodian.

The reading of this volume impressed on the reviewer that the recent fundamental progress in cytochemistry bears the hope of a solution of the problems of neoplasm growth and virus pathogenesis in the not too remote future.

A. A. A.